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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant : Michael J. Elliott et al.

Serial No. : 08/602,272 Examiner: K. Canella

Filed : February 16, 1996 Group Art Unit: 1642

For : METHODS OF PREVENTING OR TREATING THROMBOSIS WITH TUMOR NECROSIS FACTOR ANTAGONISTS

1185 Avenue of the Americas  
New York, New York 10036  
November 5, 2004

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Sir:

SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT

In accordance with the duty of disclosure under 37 C.F.R. §1.56, applicants would like to direct the Examiner's attention to the following disclosures, which are listed on Form PTO-1449 (**EXHIBIT A**). Copies of the disclosures listed below as items 1-10 are attached hereto as **EXHIBITS 1-10**, respectively.

1. PCT International Application No. WO 95/03827 A, published February 9, 1995 (Kennedy Institute Of Rheumatology) (**EXHIBIT 1**);
2. Bertini, R., et al., "Depression Of Liver Drug Metabolism And Increase In Plasma Fibrinogen By Interleukin 1 And Tumor Necrosis Factor: A Comparison With Lymphotoxin And Interferon," Int J. Immunopharmac. (1988), 19(5):525-530 (**EXHIBIT**

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2);

3. Bertini, R., et al., "Dexamethasone modulation of in vivo effects of endotoxin, tumor necrosis factor, and interleukin-1 on liver cytochrome P-450, plasma fibrinogen, and serum iron," J. Leukoc. Biol. (1989), 46(3):254-62 (**EXHIBIT 3**);
4. Gresser, I., et al., "Tumor necrosis factor induces acute phase proteins in rats," J. Biol. Regul. Homeost. Agents (1987), 1(4):173-6 (**EXHIBIT 4**);
5. Nawroth, P., et al., "Tumor Necrosis Factor/Cachectin-Induced Intravascular Fibrin Formation In Meth A Fibrosarcomas," J. Exp. Med. (1988), 168:637-647 (**EXHIBIT 5**);
6. Sekut, L., et al., "Anti-inflammatory activity of phosphodiesterase (PDE)-IV inhibitors in acute and chronic models of inflammation," Clin. Exp. Immunol. (1995), 100(1):126-32 (**EXHIBIT 6**);
7. Soria, J., et al., "Pentoxifylline, fibrinogen and leukocytes," Blood Coagul. Fibrinolysis (1990), 1(4-5):485-7 (**EXHIBIT 7**);
8. van der Poll, T., et al., "Fibrinolytic Response to Tumor Necrosis Factor in Healthy Subjects," J. Exp. Med. (1991), 174:729-732 (**EXHIBIT 8**);
9. van Hinsbergh, V.W., et al., "Progress of

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fibrinolysis during tumor necrosis factor infusions in humans. Concomitant increase in tissue-type plasminogen activator, plasminogen activator inhibitor type-1, and fibrin(ogen) degradation products," Blood (1990), 76(11):2284-9 (**EXHIBIT 9**); and

10. Zabel, P. et al., "Inhibition of endogenous TNF formation by pentoxifylline," Immunobiology (1993), 187(3-5):447-63, review ((**EXHIBIT 10**));

A European Search Report was issued on August 5, 2004 in connection with related European Application No. EP 03 02 5867.7. A copy of the August 5, 2004 European Search Report is attached hereto as **EXHIBIT B**. The above-listed reference 1 was cited in that Search Report.

The eleven remaining references cited in the enclosed European Search Report were previously submitted in a September 25, 1997 Information Disclosure Statement to the U.S. Patent and Trademark Office in connection with the instant application.

A Communication Of A Notice Of Opposition was issued on August 25, 2004 in connection with related European Application No. EP 97 90 3485.7. A copy of the August 25, 2004 Communication is attached hereto as **EXHIBIT C**. The above-listed references 2-10 were cited in that Communication.

The reference cited as "D7" in the enclosed Communication was previously cited in an August 21, 2003 Office Action in connection with the instant application.

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Pursuant to 37 C.F.R. §1.97(d)(2), the required fee for filing this Supplemental Information Disclosure Statement is ONE-HUNDRED AND EIGHTY DOLLARS (\$180.00), and a check for this amount is enclosed.

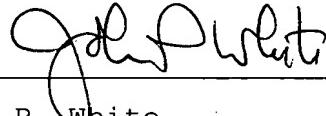
Furthermore, in compliance with 37 C.F.R. §1.97(e)(1), each item of information contained in this Supplemental Information Disclosure Statement was first cited in any communication from a foreign patent office in a counterpart foreign patent application not more than three months prior to the filing of this Supplemental Information Disclosure Statement.

If a telephone conference would be of assistance in advancing prosecution of the subject application, applicants' undersigned attorneys invite the Examiner to telephone them at the number provided below.

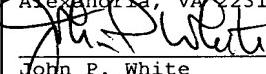
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No fee, other than the enclosed \$180.00 fee for filing a Supplemental Information Disclosure Statement, is deemed necessary in connection with the filing of this Supplemental Information Disclosure Statement. However, if any additional fee is required, authorization is hereby given to charge the amount of such fee to Deposit Account No. 03-3125.

Respectfully submitted,



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Form PTO-1449

U.S. Department of Commerce  
Patent and Trademark OfficeINFORMATION DISCLOSURE CITATION  
(Use several sheets if necessary)

Application Number	08/602,272
Filing Date	February 16, 1996
First Named Inventor	Michael J. Elliott
Art Unit	1642
Examiner Name	K. Canella
Attorney Docket No.	1481/65021/JPW/AJ M/CY

## NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and/or country where published.	T <sup>2</sup>
	2	BERTINI, R., ET AL., "Depression Of Liver Drug Metabolism And Increase In Plasma Fibrinogen By Interleukin 1 And Tumor Necrosis Factor: A Comparison With Lymphotoxin And Interferon," <u>Int J. Immunopharmac.</u> (1988), 19(5):525-530 ( <b>EXHIBIT 2</b> );	
	3	BERTINI, R., ET AL., "Dexamethasone modulation of in vivo effects of endotoxin, tumor necrosis factor, and interleukin-1 on liver cytochrome P-450, plasma fibrinogen, and serum iron," <u>J. Leukoc. Biol.</u> (1989), 46(3):254-62 ( <b>EXHIBIT 3</b> );	
	4	GRESSER, I., ET AL., "Tumor necrosis factor induces acute phase proteins in rats," <u>J. Biol. Regul. Homeost. Agents</u> (1987), 1(4):173-6 ( <b>EXHIBIT 4</b> );	
	5	NAWROTH, P., ET AL., "Tumor Necrosis Factor/Cachectin-Induced Intravascular Fibrin Formation In Meth A Fibrosarcomas," <u>J. Exp. Med.</u> (1988), 168:637-647 ( <b>EXHIBIT 5</b> );	
	6	SEKUT, L., ET AL., "Anti-inflammatory activity of phosphodiesterase (PDE)-IV inhibitors in acute and chronic models of inflammation," <u>Clin. Exp. Immunol.</u> (1995), 100(1):126-32 ( <b>EXHIBIT 6</b> );	
	7	SORIA, J., ET AL., "Pentoxifylline, fibrinogen and leukocytes," <u>Blood Coagul. Fibrinolysis</u> (1990), 1(4-5):485-7 ( <b>EXHIBIT 7</b> );	
	8	VAN DER POLL, T., ET AL., "Fibrinolytic Response to Tumor Necrosis Factor in Healthy Subjects," <u>J. Exp. Med.</u> (1991), 174:729-732 ( <b>EXHIBIT 8</b> );	
	9	VAN HINSBERGH, V.W., ET AL., "Progress of fibrinolysis during tumor necrosis factor infusions in humans. Concomitant increase in tissue-type plasminogen activator, plasminogen activator inhibitor type-1, and fibrin(ogen) degradation products," <u>Blood</u> (1990), 76(11):2284-9 ( <b>EXHIBIT 9</b> ); and	
	10	ZABEL, P. et al., "Inhibition of endogenous TNF formation by pentoxifylline," <u>Immunobiology</u> (1993), 187(3-5):447-63, review ( <b>EXHIBIT 10</b> ).	

EXAMINER  
SIGNATURE

DATE CONSIDERED

\*EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609: Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. <sup>1</sup>Applicant's unique citation designation number (optional). <sup>2</sup>Applicant is to place a checkmark here if English language Translation is attached.

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**Exhibit A**